Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States

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Prevention of Antiretroviral Drug Resistance (Updated September 14, 2011)

Panel's Recommendations
• HIV-infected pregnant women should be given combination antiretroviral (ARV) drug regimens to maximally suppress viral replication; that is the most effective strategy for preventing development of resistance and minimizing risk of perinatal transmission **(AII)**.
• All pregnant women should be counseled about the importance of adherence to prescribed ARV medications to reduce the potential for development of resistance **(AII)**.
• Pregnant women who are receiving a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based combination ARV therapy solely for prophylaxis of transmission that will be discontinued after delivery should receive nucleoside analogue agents for at least 7 days after the NNRTI is stopped to minimize risk of resistance **(AI)**. An alternative strategy is to substitute a protease inhibitor (PI) for the NNRTI prior to the interruption and to continue the PI with dual nucleoside reverse transcriptase inhibitors (NRTIs) for at least 7 days after stopping the NNRTI **(CIII)**. The optimal interval between stopping an NNRTI and the other ARV drugs is not known (see Stopping Antiretroviral Therapy during Pregnancy and Postpartum Follow-Up of HIV-Infected Women).
• Adding single-dose maternal/infant nevirapine to an ongoing combination ARV regimen given for treatment or prophylaxis does not increase efficacy in reducing perinatal transmission and may result in nevirapine drug resistance in the mother and/or infant; therefore single-dose maternal/infant nevirapine is not recommended in this situation **(AI)**.

The most effective way to prevent the development of ARV drug resistance in pregnancy is to use and adhere to an effective combination of ARV drugs to achieve maximal viral suppression.

Several studies have shown that development of nevirapine resistance is significantly decreased (but not eliminated) after exposure to single-dose intrapartum nevirapine (given alone or in combination with antenatal ART) when zidovudine/lamivudine is given intrapartum and administered for 3–7 days postpartum in women who have received single-dose nevirapine[1-3]. A variety of other regimens (e.g., tenfovir/emtricitabine, zidovudine/didanosine) given for 7–30 days postpartum following maternal single-dose nevirapine have also been shown to be very effective in reducing the development of nevirapine resistance[4-6]. An alternative strategy is to substitute a PI for the NNRTI and to continue the PI with dual NRTIs for a period of time[7]. The optimal duration for continuation of either dual nucleosides or the substituted PI-based regimen after stopping the NNRTI is unknown. NNRTI drugs have long half-lives, and drug levels can persist for up to 1–3 weeks after stopping the drug; efavirenz levels persist longer than nevirapine levels[8-9]. More research is needed on the optimal duration of time and regimen to "cover" this period of prolonged NNRTI exposure to prevent the emergence of resistance after discontinuation of NNRTI-based therapy. Many experts will stop the NNRTI drug and continue the other ARV drugs for at least 7 days, although other experts would recommend up to 30 days, particularly if an efavirenz-based regimen is being discontinued.

References

1. McIntyre JA, Hopley M, Moodley D, et al. Efficacy of short-course AZT plus 3TC to reduce nevirapine resistance in the prevention of mother-to-child HIV transmission: a randomized clinical trial. *PLoS Med.* Oct 2009;6(10):e1000172.
2. Chaix ML, Ekouevi DK, Rouet F, et al. Low risk of nevirapine resistance mutations in the prevention of mother-to-child transmission of HIV-1: Agence Nationale de Recherches sur le SIDA Ditrame Plus, Abidjan, Cote d'Ivoire. *J Infect Dis.* Feb 15 2006;193(4):482-487.
3. Farr SL, Nelson JA, Ng'ombe TJ, et al. Addition of 7 days of zidovudine plus lamivudine to peripartum single-dose nevirapine effectively reduces nevirapine resistance postpartum in HIV-infected mothers in Malawi. *J Acquir Immune*

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Defic Syndr. Aug 15 2010;54(5):515-523.

4. Arrive E, Chaix ML, Nerrienet E, et al. Maternal and nenonatal tenofovir and emtricitabine to prevent vertical transmission of HIV-1: tolerance and resistance. *AIDS.* Oct 23 2010;24(16):2481-2488.
5. Lallemant M, Ngo-Giang-Huong N, Jourdain G, et al. Efficacy and safety of 1-month postpartum zidovudine-didanosine to prevent HIV-resistance mutations after intrapartum single-dose nevirapine. *Clin Infect Dis.* Mar 15 2010;50(6):898-908.
6. Van Dyke R, Jourdain G, Shapiro D, al. e. A Phase II Study of the Incidence of Nevirapine Resistance Mutations in HIV-infected Thai Women Receiving a Single Intrapartum Dose of NVP followed by a Postpartum Tail of ZDV/ddI or ZDV/ddI/LPV/r: IMPAACT P1032. *16th Conference on Retroviruses and Opportunistic Infections. Montreal,* Canada 2009.
7. Fox Z, Phillips A, Cohen C, et al. Viral resuppression and detection of drug resistance following interruption of a suppressive non-nucleoside reverse transcriptase inhibitor-based regimen. *AIDS.* Nov 12 2008;22(17):2279-2289.
8. Cressey TR, Jourdain G, Lallemant MJ, et al. Persistence of nevirapine exposure during the postpartum period after intrapartum single-dose nevirapine in addition to zidovudine prophylaxis for the prevention of mother-to-child transmission of HIV-1. *J Acquir Immune Defic Syndr.* Mar 1 2005;38(3):283-288.
9. Sadiq ST, Fredericks S, Khoo SH, Rice P, Holt DW. Efavirenz detectable in plasma 8 weeks after stopping therapy and subsequent development of non-nucleoside reverse transcriptase inhibitor-associated resistance. *AIDS.* Oct 14 2005;19(15):1716-1717.

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